Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
A41352A		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2004/008254	07.06.2004	06.06.2003
International Patent Classification (IPC) or national classification and IPC		
Applicant		
ASAHI KASEI MEDICAL CO., LTD.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 14 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 2 sheets, as follows:

      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))

      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2004/008254

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:

pages 1-27 as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ the claims:

nos. 1,3-23,25-90 as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* 2,24 received by this Authority on 30.11.2004

nos.* _____ received by this Authority on _____

☒ the drawings:

sheets 1/1 as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

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Box No. III **Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 83-90

because:

☒ the said international application, or the said claims Nos. 83-90
relate to the following subject matter which does not require an international preliminary examination (*specify*):

Claims 83 to 90 include configurations that are related to a method for the treatment of the human body by means of therapy, and thus relate to a subject matter for which this International Preliminary Examining Authority is not required to carry out an international preliminary examination under the provisions of PCT Article 34(4)(a)(i) and PCT Rule 67.1(iv).

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 83-90

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
☐ has not been furnished
☐ does not comply with the standard

the computer readable form
☐ has not been furnished
☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

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Box No. IV **Lack of unity of invention**

1. ☐ In response to the invitation to restrict or pay additional fees the applicant has:
   - ☐ restricted the claims.
   - ☒ paid additional fees.
   - ☐ paid additional fees under protest.
   - ☐ neither restricted the claims nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:
   - ☐ complied with.
   - ☒ not complied with for the following reasons:

[1] Claims 1 to 4, 24 to 60 and 61
(hereinafter, invention group 1)
[2] Claims 5 to 7
(hereinafter, invention group 2)
[3] Claims 62 to 81 and 82
(hereinafter, invention group 3)

(1) Invention groups 1 and 2 share the common feature of being related to a material for promoting wound healing that comprises a porous sheet material as one constituent component, or to a method for the production thereof.

[Refer to the Supplemental Box]

4. Consequently, this report has been established in respect of the following parts of the international application:
   - ☐ all parts.
   - ☒ the parts relating to claims Nos. 1-82

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-82	YES
	Claims		NO
Inventive step (IS)	Claims	1-82	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-82	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Document 1: JP 7-59840 A (Terumo Corp.), 07 March 1995, entire text, claims and examples 4 and 5 (Family: none)

Document 2: JP 2002-531532 A (Johnson & Johnson Medical Ltd.), 24 September 2002, entire text, claims and examples & GB 2345519 A & WO 00/33893 A1 & AU 2000/15770 B & EP 1053029 A1

Document 3: JP 8-224293 A (Sanfaibu Kabushiki Kaisha), 03 September 1996, entire text, claims and examples 1 and 2 (Family: none)

Document 4: JP 5-43453 A (Sumitomo Pharmaceuticals Co., Ltd.), 23 February 1993, entire text, claims and examples 1 to 3 (Family: none)

Document 5: JP 6-500802 A (AMGEN INC.), 27 January 1994, entire text and claims & EP 518697 A2 & WO 92/22304 A2 & AU 9221926 B & US 5418222 A

Document 6: JP 2003-10301 A (Ed Geistlich Söhne AG Für Chemische Industrie), 14 January 2003, entire text & EP 1252903 A1 & AU 2002/35618 B & CA 2383636 A1 & US 2002/160036 A

Document 7: US 5510102 A (Univ. of California), 23 April 1996, entire text & WO 96/23039 A1

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Document 8: JP 11-239609 A (Sekisui Chemical Co., Ltd.), 07 September 1999, entire text (Family: none)

Document 9: WO 96/27397 A1 (Quantic Biomedical Partners), 12 September 1996, entire text and claims & AU 9654166 B & EP 813427 A1 & JP 11-502435 A

Document 10: JP 2003-524590 A (Cytomedix Inc.), 19 August 2003, entire text & WO 99/66923 A1 & GB 2342046 A & AU 9953122 B & EP 1091735 A1 & US 6303112 A

Document 11: JP 2001-508807 A (Bio-Products & Bio-Engineering AG.), 03 July 2001, entire text & WO 99/24044 A1 & AU 9911354 B & EP 966293 A1 & US 2002/1624 A

Document 12: JP 62-501628 A (Curatech, Inc.), 02 July 1987, entire text & WO 86/3122 A1 & AU 8550949 B & EP 202298 A1 & CA 1261259 A1 & GB 2248777 A & US 5165938 A

Document 13: C. KALKA et al., "Transplantation of ex vivo expanded endothelial progenitor cells for therapeutic neovasculatization," Proc. Natl. Acad. Sci. USA, 2000, Vol. 97, No. 7, pages 3422 to 3427

Document 14: Y ZHAO et al., "A human peripheral blood monocyte-derived subset acts as pluripotent stem cells," Proc. Natl. Acad. Sci. USA, 04 March 2003, Vol. 100, No. 5, pages 2426 to 2431

Document 15: M. VALBONESI et al., "The role of autologous fibrin-platelet glue in plastic surgery: a preliminary report," Int. J. Art. Organs.,

2002, Vol. 25, No. 4, pages 334 to 338

Document 16: JP 2001-204807 A (Gunze Ltd.), 31 July 2001, entire text (Family: none)

Document 17: JP 2002-47299 A (Terumo Corp.), 12 February 2002, entire text (Family: none)

Document 18: JP 7-507558 A (INOTEB), 24 August 1995, entire text & WO 93/25215 A1 & FR 2691911 A1 & EP 643582 A1 & US 5618663 A

Document 19: WO 99/58172 A1 (Asahi Medical Co., Ltd.), 18 November 1999, entire text & AU 9937297 B & EP 1080741 A1 & US 6699388 A

Document 20: US 6049026 A (Cleveland Clinic Found.), 11 April 2000, entire text & WO 99/59500 A2 & AU 99/41994 B & EP 1085842 A2 & JP 2002-515288 A

Document 21: WO 01/91880 A1 (Baxter Int. Inc.), 06 December 2001, entire text & WO 02/3909 A1 & AU 2001/63488 B & AU 2001/69493 B & US 2002/113003 A & EP 1300128 A1 & EP 1309384 A1 & US 2003/209479 A

Sheet-like compositions that are effective for healing wounds and the like, which are configured by supporting a component that is capable of exhibiting a cell proliferation action upon a porous sheet material such as a collagen sponge or a nonwoven fabric, were well known prior to the priority date of the present application, as disclosed in documents 1 to 6.

In addition, documents 7 to 15 indicate that leukocytes and/or blood platelets are effective as therapeutic components in medicinal compositions for healing wounds, and documents 16 to 18 disclose the

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

feature of using animal cells such as blood platelets as a medicament or as a component that is associated with a treatment, wherein said cells have been supported upon a porous sheet material for use. Furthermore, the feature of trapping leukocytes and/or blood platelets upon a porous sheet material by employing a commonly used blood filter that has a porous sheet material and subjecting blood to a filtration process can be considered to have been well known prior to the priority date of the present application, as disclosed in documents 19 to 21.

However, the feature wherein living cells such as leukocytes and/or blood platelets, which are capable of producing growth factors, are supported upon a porous sheet material and then said sheet material is directly applied to the site of a wound as a material for promoting wound healing in order to impart a favorable effect whereby the healing of wounds is promoted is not specifically indicated in any of documents 1 to 21, and said feature cannot be said to have been obvious to a person skilled in the art in the light of the documents in question.

Box No. VIII **Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

(A)

With regards to the device that is set forth in claim 62, it is not sufficiently clear whether or not the device itself or a constituent element thereof serves as the material for promoting wound healing; likewise, the manner in which the device is used and the nature of the process for producing the material for promoting wound healing are not sufficiently clear.

(The present report expresses an opinion based on the results of a search of the prior art in relation to a device which injects blood via the intake port for injection, captures leukocytes and/or blood platelets upon a porous sheet material and then produces a material for promoting wound healing from the resulting porous sheet material as the invention that is set forth in claim 62).

(2)

With regards to the materials for promoting wound healing which are set forth in claims 1 to 82 (hereinafter, simply referred to as 'the materials from the present invention'), there cannot be considered to be any specific disclosures in relation to a configuration for the application the materials from the present invention in the claims; however, the description presents a configuration wherein said materials are applied to the site of a wound as an patch along with preliminary experimental data pertaining to the actual actions and effects with regards to the healing of wounds.

Box No. VIII Certain observations on the international application

In addition, among the significant actions of the materials set forth in claims 1 to 82 which are indicated by the applicant in the written response, the assertions that:

- in comparison to the configurations that are disclosed in the prior art documents wherein only therapeutic components such as proteins or the like are supported upon a porous sheet material, configurations wherein living cells are supported upon a porous sheet material will exhibit a superior wound-healing effect as a result of the interaction between the condition of the wound and the surrounding environment; and
- the materials from the present invention exhibit superior shape conformance characteristics in relation to the site of a wound and superior machining strength characteristics as a result of being configured from a porous sheet material,

for example, demonstrate that among the materials from the present invention, materials with a configuration other than that of a patch which is applied to the site of a wound cannot be said to be fully supported by the description in the meaning of PCT Article 6 and cannot be said to be disclosed within the description in a manner sufficiently clear and complete for the invention to be carried out by a person skilled in the art in the meaning of PCT Article 5.

Furthermore, with regards to the materials that are set forth in claims 5 and 6, which are capable of producing growth factors, only the inventions pertaining to a material that is configured by supporting living

Box No. VIII **Certain observations on the international application**

cells from blood, such as leukocytes and/or blood platelets, upon a porous sheet material can be said to be fully supported by the description in the meaning of PCT Article 6 and to be disclosed within the description in a sufficient manner in the meaning of PCT Article 5.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

Box IV

However, materials for promoting wound healing that are configured from a porous sheet material, said materials for promoting wound healing being configured by including a substance that is considered to be a therapeutic component with a cell proliferation potency that contributes to the healing of wounds within said sheet material, can be considered to have been well known prior to the priority date of the present application, as disclosed in documents that had been disseminated prior to the priority date of the present application, such as, for example:

JP 7-59840 A (Terumo Corp.), 07 March 1995, entire text, claims, examples and test examples (Family: none);

JP 5-43453 A (Sumitomo Pharmaceuticals Co., Ltd.), 23 February 1993, entire text, claims, examples and test examples (Family: none);

JP 8-224293 A (Sanfaibu Kabushiki Kaisha), 03 September 1996, entire text, claims, paragraphs [0003] and [0022], and examples (Family: none); and

JP 6-500802 A (AMGEN INC.), 27 January 1994, entire text and examples 1 to 7 & EP 518697 A2 & WO 92/22304 A1 & AU 9221926 B & US 5418222 A.

Supplemental Box

Therefore, the abovementioned feature that is common to invention groups 1 and 2 cannot be said to have been a special technical feature at the time the present application was filed.

With regards to the material for promoting wound healing, the invention groups have respective features that characterize the inventions; for example,

- Invention Group 1:

is characterized by the feature wherein the material for promoting wound healing comprises leukocytes and/or blood platelets (hereinafter, invention characterizing feature 1); and

- Invention Group 2:

is characterized by the feature wherein the material for promoting wound healing is capable of producing growth factors (hereinafter, invention characterizing feature 2).

However, it is apparent from a comparison of only invention characterizing features 1 and 2 that the features in question cannot be considered to have a special technical feature in common.

As a result, the optional configurations of the inventions from invention group 1 and the optional configurations of the inventions from invention group 2 cannot be said to have a relationship that involves the same special technical feature; therefore, invention group 1 and invention group 2 cannot be considered to be

so linked as to form a single general inventive concept.

In addition, the disclosures of claims 8 to 23 cite both the inventions from invention group 1 and the inventions from invention group 2 within the same claim; therefore, the disclosures of claims 8 to 23 are considered to include two inventions that are not linked so as to form a single general inventive concept, for the same reasons as are indicated above.

(2)

The inventions set forth in the claims of invention group 3 can be considered to share a common invention characterizing feature, i.e. the device for preparing the material for promoting wound healing, which is set forth in claim 62. However, the disclosure of claim 62 cannot be considered to include any mention of the relationship between the porous sheet material and the material for promoting wound healing, and does not clearly indicate whether said porous sheet material has been configured so as to exhibit the abovementioned invention characterizing feature 1 and/or the abovementioned invention characterizing feature 2.

As a result, invention group 3 cannot be said to comprise only inventions that share the special technical feature of invention group 1 or invention group 2; therefore, invention group 3 cannot be said to be so linked as to form a single inventive concept in relation to either invention group 1 or invention group 2.